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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/134,771	08/12/1998	DINAH W.Y. SAH	860098.425	8421

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Pennie & Edmonds
1155 Avenue of the Americas
New York, NY 10036-2711

EXAMINER
KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
1636	32

DATE MAILED: 04/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Advisory Action	Application No.	Applicant(s)	
	09/134,771	SAH ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 20 March 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *20 March 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1-10,13-15 and 23-27*.

Claim(s) withdrawn from consideration: _____.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☒ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). *27*.

10.☐ Other: _____

JEFFREY FREDMAN
PRIMARY EXAMINER

Continuation of 5. does NOT place the application in condition for allowance because:

Claims 1-10, 13-15 and 23-27 stand rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Hosimaru et al (PNAS. 93:1518-1523, 1996, *ref of record*) and Prasad et al (In Vitro. Cell Dev. 30A:596-603, 1994, *ref of record*) in view of Boss et al (US 5411883, 1995, *ref of record*), Weiss et al (US 5750376) and Gallyas et al (Neurochem. Res. 22(5):569-575, 1997, *ref of record*) for the same reasons of record as set forth in the office action mailed on 09/20/02.

Response to arguments

The applicant argues that there is no suggestion or motivation to combine the cited references and there is no reasonable expectation of success. The applicant argues that one would not have been motivated to make immortalized human mesencephalon progenitor cells in view of Hosimaru and Prasad, since Boss does not suggest the immortalization of human mesencephalon progenitor cells (response, pages 3-4). In addition the applicant argues that the cited references do not teach every limitation of the claimed invention. The applicant argues that combination of the cited references do not teach differentiation of mesencephalon cells with combination of growth factors including forskolin, GDNF, CNTF, IGF-1 and BDNF (response pages 4-6). The applicant argues that Hosimaru teaches away from the use of forskolin or any other factor to differentiate the progenitor cells. The applicant argues that Weiss teaches that the combination of EGF or FGF-2 with PDGF has different purpose and achieves a different result than in the instant invention. The applicant argues that Boss does not teach cells that grow as a monolayer (response pages 6). The applicant concluded that rat cells are composition of matter that is different from human cells, therefore invention as claimed is not obvious over cited prior art of record. (response page 7).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

The applicant fails to consider the combined teaching of the reference cited herein in entirety. The combination and modification of the teachings of the prior art clearly suggested the claimed invention. The arguments taken as a whole rely heavily on the deficiencies of each reference taken alone. One cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In this case, Hosimaru teaches immortalized rat neuronal progenitor cells wherein the expression of v-myc oncogene is driven by a tetracycline-controlled trnsactivator and a human cytomegalovirus (CMV) promoter. The cited art teaches that cells were first cultured in a serum supplemented media follow by culturing in serum free media containing growth factors. Hosimaru et al teaches the culturing and selection of the cells onto polyornithine/laminin-coated tissue culture plates. In addition, Hosimaru et al further teaches that presence of several cytokine, forskolin or growth factors is required for the differentiation of immortalized neuronal precursor cells (page 1518, abstract; page 1519, col.1. para.3; page 1522, col.1, para.2). Prasad et al teaches the isolation of an immortalized dopamine-producing nerve cell line derived from fetal rat mesencephalic tissue transfected with an oncogene. Prasad clearly teaches that mesencephalic cell could be genetically manipulated (see abstract).

Boss teaches the isolation and culture methods for the proliferation of human mesencephalon neuron progenitor cells, wherein the cultured neuronal cells differentiate to produce dopamine-producing

cells (see abstract; col.6, line 33; col.9-10, table 1-3; col.20 line 60). In addition, Boss et al clearly teaches the isolation and monolayer culture of human mesencephalon neuron progenitor cells in details (see abstract; and preparation of monolayer culture, col.11 line 25).

Weiss teaches a method for producing genetically modified multipotent neuronal stem cells (mouse monkey and human) and their progeny. The cited art teaches the use a combination of proliferation inducing growth factors selected from NGF, BDNF, NT-3, NT-4, NT-5, CNTF, FGF-1, FGF-2, EGF TGFa, TGFb, PDGF, IGFs and interleukins (col. 17, line 1-15; col.22, line 17-29). The cited art further teaches in-vitro proliferation of neuronal progenitor cells in the presence of above mentioned growth factors (col. 30 line 17; col.31, lines 46-64, examples 1-8

Gallyas et al teaches the characterization of mouse immortalized neuronal cell lines by measuring the concentration of various neurotransmitters, like GABAergic and dopamine (see abstract; page 570, col.2, para 3; page 571, table-I, fig-1; page 572, table-II). Gallyas clearly provides method to characterize neuronal cells by the identification of GABAergic and dopamine expression as required by claim 7 and 8 of instant invention.

The cited art clearly anticipate the invention as claimed because the composition and functions as claimed are presumed inherent. The composition is physically the same it must have the same properties. "Products of identical chemical composition can not have mutually exclusive properties."A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) see MPEP § 2112.02. In instant case mammalian mesencephalon neuron progenitor cells (mouse and human) are considered to have identical characteristics, therefore the genetic modification and culturing of human mesencephalon neuron progenitor with combination of know growth factors is not an unexpected finding especially in view of cited prior art of record.

Thus, it would have been obvious to one ordinary skill in the art at the time the invention was made to substitute the immortalized rat neuronal progenitor cells as taught by Hosimaru et al and Prasad et al with human mesencephalon neuron progenitors cells (Boss et al). It would have been further obvious to characterize immortalized human mesencephalon cells as taught by Gallyas et al because dopamine and GABA are neurotransmitter of interest. It would have been further obvious to use a combination of BDNF, CNTF, FGF-2, EGF, PDGF, and IGFs to promote the survival of mesencephalonic dopaminergic neurons in view of Weiss. One would have been motivated to make immortalized human neuronal progenitor cells wherein the expression of v-myc oncogene is driven by tetracycline-controlled trnsactivator because the suppression of v-myc oncogene in an immortalized progenitor induces the differentiation of the neuronal progenitor cell. Furthermore, immortalized human neuronal progenitor cells are valuable research tools to understand the molecular mechanism that control the development and function of nervous system cells in-vitro. In addition, one would have a reasonable expectation of success because neuronal progenitor cells are easy to transfect, especially in the presence of proliferation enhancing growth factors, which promotes cell survival. Furthermore, in view of cited art phenotypic characterization of GABAergic and dopaminergic neuronal cells has been considered routine in the art at the time of filing. Thus, the invention as claimed is prima facie obvious in view of prior art of record.

S. Kaushal
PATENT EXAMINER